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Association of Foot Symptoms With Decreased Time to All-Cause Mortality: The Johnston County Osteoarthritis Project

Skylar Harmon,[1] Carolina Alvarez,[2] Marian T. Hannan,[3] Leigh F. Callahan,[2] Lucy S. Gates,[4] Catherine J. Bowen,[5] Hylton B. Menz,[6] Amanda E. Nelson,[2] and Yvonne M. Golightly[7]

Objective. Adults with foot symptoms (ie, pain, aching, or stiffness) may be at increased risk of reduced time to all-cause mortality. The purpose of this study was to evaluate whether foot symptoms are independently associated with all-cause mortality in older adults.

Methods. We analyzed longitudinal data from 2613 participants from the Johnston County Osteoarthritis Project, a longitudinal population-based cohort of adults 45 years of age and older. Participants completed questionnaires at baseline to determine presence of foot symptoms and covariable status. Baseline walking speed was measured via an 8-foot walk test. To examine the association of foot symptoms with time to mortality, hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using Cox regression models, adjusted for potential confounders.

Results. We observed 813 deaths over 4 to 14.5 years of follow-up. At baseline, 37% of participants had foot symptoms, mean age was 63 years, mean body mass index was approximately 31 kg/m^2, 65% were women, and 33% were Black. Moderate to severe foot symptoms were associated with reduced time to mortality after adjustment for demographics, comorbidities, physical activity, and knee and hip symptoms (HR = 1.30, 95% CI 1.09–1.54). Importantly, this association was not modified by walking speed or diabetes.

Conclusion. Individuals with foot symptoms had an increased hazard of all-cause mortality compared with those with no foot symptoms. These effects were independent of key confounders and were not moderated by walking speed. Effective interventions to identify and manage at least moderate foot symptoms may reduce the risk of decreased time to mortality.

INTRODUCTION

As many as one in three middle-aged to older adults have foot symptoms (ie, pain, aching, or stiffness on most days) (1,2), with greater prevalence among women, persons who identify as Black, those who are obese, those of older age, and those with routine/manual occupations (3). Foot symptoms are associated with decreased physical function and disability, even when controlling for important covariates (1,4–6). Foot symptoms pose a burden that likely affects locomotor function and participation in daily physical, occupational, and social activities, making it a significant public health concern (7,8).

Previous studies have highlighted the association of knee or hip symptoms with all-cause mortality. In 2018, Cleveland et al examined the impact of knee symptoms on excess mortality using data from the Johnston County Osteoarthritis Project (JoCoOA) (9). The investigators found that knee symptoms in the presence or absence of radiographic osteoarthritis (OA) were associated with an increase in all-cause mortality of greater than 15%. Among patients with knee or hip symptoms with OA,

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[1]Skylar Harmon, BA: University of North Carolina at Chapel Hill, Chapel Hill, and Nova Southeastern University and Dr. Kiran C. Patel College of Allopathic Medicine, Fort Lauderdale, Florida; [2]Carolina Alvarez, MS, Leigh F. Callahan, PhD, Amanda E. Nelson, MD, MPH: University of North Carolina at Chapel Hill, Chapel Hill; [3]Marian T. Hannan, DSc, MPH: Harvard T. H. Chan School of Public Health, Beth Israel Deaconess Medical Center, and Harvard Medical School, Boston, Massachusetts; [4]Lucy S. Gates, PhD: University of Southampton and Southampton General Hospital, Southampton, UK; [5]Catherine J. Bowen, PhD: University of Southampton, Southampton, UK; [6]Hylton B. Menz, PhD, DSc: La Trobe University, Bundoora, Victoria, Australia; [7]Yvonne M. Golightly, PT, PhD: University of North Carolina at Chapel Hill, Chapel Hill, and University of Nebraska Medical Center, Omaha.

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Address correspondence via email to Yvonne M. Golightly, PT, PhD, at ygolightly@unmc.edu.

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SIGNIFICANCE & INNOVATIONS

- Foot symptoms (ie, pain, aching, stiffness) are common among middle-aged to older adults, limiting physical function, physical activity, and quality of life.
- Symptoms at the knee and hip are linked to reduced time to all-cause mortality, but the role of foot symptoms in mortality has not been established.
- The present study provided novel results demonstrating that moderate to severe foot symptoms were related to a higher hazard of all-cause mortality, and this relationship was independent of walking speed, sex, race, obesity status, or diabetes status.
- Strategies to prevent and treat moderate to severe foot symptoms may improve physical function and activity, thus affecting mortality outcomes.

Nüesch et al reported excess all-cause mortality [standardized mortality ratio 1.55, 95% confidence interval (CI) 1.41–1.70] (10). Several other studies have also shown associations between knee symptom presence and 35% to 37% reduced time to mortality (11). Additionally, Cleveland et al reported an increased hazard of 1.3 for all-cause mortality in participants with hip symptoms without radiographic OA compared with participants with neither radiographic OA nor symptoms at the hip [adjusted hazard ratio (aHR) = 1.28, 95% CI 1.13–1.46] (12).

Walking speed is an important metric for evaluating current health and future health outcomes (13). Master et al found that adults with symptomatic knee radiographic OA (Kellgren-Lawrence grade ≥2) had increased risk of mortality and that walking speed modified this relationship (14). Specifically, slower walking speeds measured at both short (2.4-meter) and standard (20-meter) distances were associated with higher mortality [aHR (95%CI) 1.23 (1.10–1.39) and 1.25 (1.09–1.43), respectively] (14). This suggests that impaired mobility resulting from symptoms may be a cause of excess mortality independent of age and comorbid conditions. Although these studies highlight the potential association of knee and/or hip symptoms with mortality, the association of foot symptoms with mortality has not been explored in detail.

Foot symptoms may contribute to less physical activity and loss of physical function, which over time could lead to factors that impact mortality, including comorbid conditions from increasing body mass or falls from muscle weakness or impaired balance. One prior study has evaluated the association of foot symptoms with self-reported and performance-based measures of physical function in the JoCoOA cohort (1), finding that the presence of foot symptoms was significantly associated with worsened mobility (slower 8-foot walk time) irrespective of knee and hip symptoms and OA. Because of the significant impact of foot symptoms on mobility, it is important to consider whether the presence of foot symptoms alone leads to reduced time to mortality. Further, there may be individuals with foot symptoms who are at a higher risk of mortality, such as those who walk at slower speeds (13), and assessment of effect modification could assist with identifying these subgroups.

Thus, the purpose of this study was to determine whether foot symptoms are associated with reduced time to all-cause mortality, and if so, whether this association is modified by reduced walking speed using the JoCoOA cohort. Our hypotheses were that foot symptoms would be linked to reduced time to mortality and that slower walking speed would amplify the magnitude of this association.

METHODS

Study participants

Participants were from the JoCoOA cohort, a longitudinal, community-based study of the occurrence of OA in Black and White civilian, noninstitutionalized adults 45 years or older who resided in a mostly rural county in North Carolina, USA. Detailed descriptions of JoCoOA eligibility criteria have been published in other literature (15). Briefly, participants in the Original Cohort were recruited during 1991–1997, and they completed follow-up visits in 1999–2004, 2006–2010, and 2013–2015. Additional participants were enrolled during 2003–2004 (Enrichment Cohort), and they completed follow-up visits in 2006–2010 and 2013–2015.

Questions about foot symptoms were not added to JoCoOA until 1999. Thus, the present study only included those Original Cohort and Enrichment Cohort participants who attended a clinic visit during 1999–2004 and had available foot symptoms data. First and second follow-up visits for the present study were defined as 2006–2010 and 2013–2015, respectively. The JoCoOA has been continuously approved by the University of North Carolina Institutional Review Board (#92-0583).

Study outcome

All-cause mortality: Excluding those who had died prior to baseline, time to all-cause mortality was quantified from the date of the initial foot examination visit (1999–2004) to the date of death. All participants had vital status assessed at each follow-up time point. Deaths were primarily found through the National Death Index (NDI) records, although some known deaths, if not found in the NDI, were confirmed through the Johnston County Register of Deeds office.

Study exposure

Foot symptoms. Foot symptoms were considered present if a participant responded "yes" to the question: "On most days,

do you have pain, aching, or stiffness in your left/right foot?" The time framing of this question varied. At baseline participants were asked to recall over the past month, at first follow-up (T2) over the past year, and at second follow-up (T3) in any one month of the past year. These symptoms were queried by presence in either foot (ie, yes or no), and also by any foot symptom laterality (ie, none, unilateral, or bilateral). Finally, symptom severity in either foot was assessed on the following scale: 0 = none, 1 = mild, 2 = moderate, and 3 = severe. The scale was used to create a severity count summed across both feet (range 0–6).

Potential confounders

Short distance walk test. At the baseline examination, walking speed was assessed from an 8-foot walk test at usual pace over an unobstructed course. The same testing was used at follow-up exams. At each examination, time was measured using a digital stopwatch and recorded to the nearest tenth of second in two trials over the 8-foot distance. Walking speed was calculated as the total distance 8 feet (2.4 meters) divided by the time to complete the walk test; the average walking speed of the two trials was calculated and used in analyses. Among older adults, the 8-foot walk test has been shown to have fair to good retest reliability (intraclass correlation coefficients >0.5) for assessing walking speed (16,17). Walking speed was grouped into categories of 1.0 m/s or faster, 0.8 to less than 1 m/s, 0.4 to less than 0.8 m/s, and less than 0.4 m/s or unable, a scale adapted from (18).

We considered the following static variables to be potential confounders because they may be associated with foot conditions and with mortality: self-reported race (Black or White), sex (female vs. male), age (in years), and education (categorized as <12 years vs. ≥12 years of school). Additional time-varying covariables included clinically measured body mass index (BMI) (in kg/m^2), ever smoker (self-reported, yes/no), any alcohol use (self-reported, yes/no), meeting the US Department of Health and Human Services guidelines for moderate/vigorous physical activity (MVPA) equal to or more than 150 minutes/week (self-reported, yes/no), current nonsteroidal anti-inflammatory drug (NSAID) use (presentation of medication container by participant or self-report, yes/no), and any report of symptoms in the hips or knees. Comorbidities assessed by self-report included history of cardiovascular disease (CVD), hypertension (HTN), liver disease, depression, and cancer, analyzed as reporting at least one of five of the listed comorbidities. Diabetes mellitus was separated from the overall comorbidity count because of its effects on foot symptoms (eg, peripheral neuropathy). Because calendar effects could impact the outcome of mortality and other risk factors in these analyses, models were stratified by decade of birth cohort.

The following variables were considered to be potential effect modifiers because of their differences affecting mortality or foot symptoms. Sex was tested for effect modification because previous studies have shown an increased incidence of foot symptoms in females compared with males (2,3). Race was tested because Black participants of JoCoOA have been shown to have higher rates of foot symptoms (19). Obesity was also considered because it has been associated with presence of nonspecific foot pain in the general population (20). Diabetes is not only implicated in foot symptoms through peripheral neuropathy but also has been shown to be a predictor of excess mortality (10,21). Walking speed was the main effect modifier we were interested in investigating because more severe walking disability has been associated with higher risk of mortality in previous studies (10).

Statistical analysis

At baseline and at follow-up time points, descriptive statistics were calculated. Continuous variables were described using means and SDs (±SD), and categorical variables were presented as frequencies and percentages. All tests were two-sided, and statistical significance was set at the 0.05 level. All analyses were conducted using SAS software version 9.4 (Cary, NC).

Participant information from baseline, first follow-up, and second follow-up was included for the above-described covariables and foot symptom definitions. Follow-up time was calculated as the time difference between baseline and confirmed death or censoring (ie, loss to follow-up or end of study on December 31, 2015).

Survival curves. We used Kaplan-Meier methods to generate nonparametric survival curves by baseline foot symptoms status strata, and the log-rank test was used to test difference by strata. We examined the association of foot symptoms over time with all-cause mortality by calculating aHRs and 95% CIs using time-dependent Cox proportional hazards regression employing the counting process to include time-varying covariables. Each model was adjusted for potential confounders.

Models. Models are presented for each of the six aspects of our study foot symptom definitions, along with three aspects of model building with covariables. Model 1 adjusted for demographics including birth cohort (as a stratum by decade), enrollment wave (original or enrichment), age, sex, race and ethnicity, and education. Model 2 adjusted for covariables in model 1 as well as comorbidities and relevant clinical risk factors including NSAIDs, smoking, alcohol use, meeting MVPA guidelines, BMI, diabetes, at least one comorbidity out of five comorbidities, knee symptoms, and hip symptoms. Model 3 adjusted for covariables in model 2 and walking speed categories.

Missing data. Covariable information for at least one measure was missing for 6.2% of participants (Figure 1). Multiple imputation was used to impute missing values with missing information assumed to be missing at random. Logistic and linear regression models were used to impute binary and continuous covariable

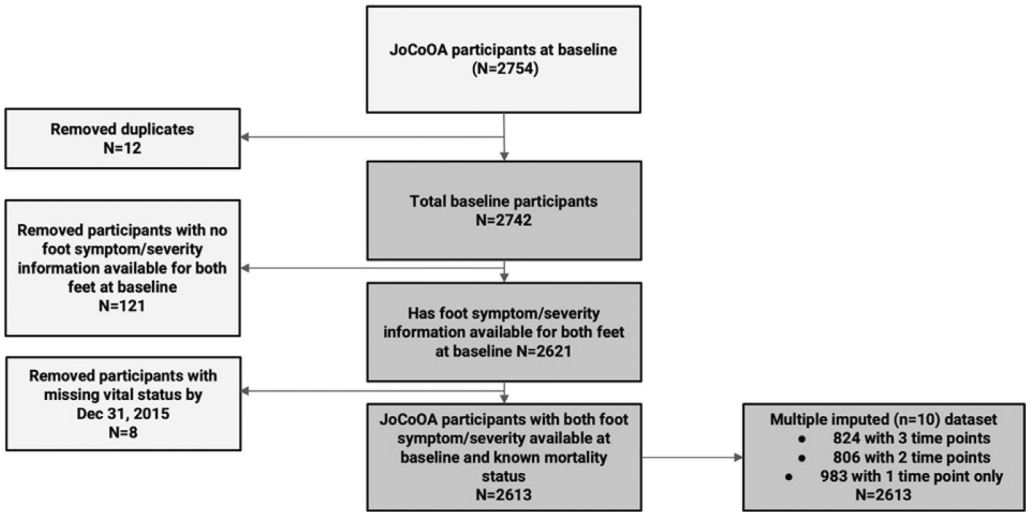


Figure 1. Analytic sample size for JoCoOA participants with baseline foot symptoms data and known mortality status. Abbreviation: JoCoOA = Johnston County Osteoarthritis Project.

Table 1. Baseline demographic characteristics, the Johnston County Osteoarthritis Project*

	Baseline (1999–2004; n = 2,613)	First follow-up (2006–2010; n = 1,604)	Second follow-up (2013–2015; n = 850)
Demographics at baseline			
Enrichment 2003–2004 cohort, n (%)	999 (38.2)	572 (35.7)	320 (37.6)
Age, years, mean ± SD	63.4 ± 10.5	68.4 ± 9.1	71.4 ± 7.7
Female sex, n (%)	1,704 (65.2)	1,069 (66.6)	574 (67.5)
Black, n (%)	856 (32.8)	492 (30.7)	280 (32.9)
<12 years education, n (%) (missing n = 12)	716 (27.4)	341 (21.3)	119 (14.0)
Time-varying variables			
BMI (kg/m^2), mean ± SD (missing n = 4)	30.6 ± 6.7	31.3 ± 7.2	31.0 ± 6.6
Ever smoker, n (%) (missing n = 121)	1,058 (40.5)	865 (53.9)	462 (54.4)
Any alcohol use, n (%) (missing n = 95)	957 (36.6)	658 (41.0)	348 (40.9)
≥150 MVPA min/week, n (%) (missing n = 3)	791 (30.3)	341 (21.3)	145 (17.1)
NSAID use, n (%) (missing n = 1)	1,259 (48.2)	1,082 (67.5)	584 (68.7)
HTN, n (%)	1,265 (48.4)	1,087 (67.8)	690 (81.2)
CVD, n (%) (missing = 1)	575 (22.0)	566 (35.3)	364 (42.8)
Diabetes, n (%)	425 (16.3)	383 (23.9)	253 (29.8)
Depression, n (%)	344 (13.2)	187 (11.7)	101 (11.9)
Liver disease, n (%)	36 (1.4)	32 (2.0)	22 (2.6)
Cancer, n (%)	28 (1.1)	41 (2.6)	81 (9.5)
Five comorbidity count: HTN, CVD, depression, liver disease, cancer, n (%) (missing n = 1)			
0	985 (37.7)	331 (20.6)	101 (11.9)
1	1,100 (42.1)	734 (45.8)	337 (39.6)
2	442 (16.9)	446 (27.8)	325 (38.2)
3	78 (3.0)	86 (5.4)	77 (9.1)
4–5	7 (0.2)	7 (0.5)	10 (1.2)
Any knee symptoms, n (%) (missing n = 2)	1,321 (50.6)	608 (37.9)	325 (38.2)
Any hip symptoms, n (%) (missing n = 3)	1,005 (38.5)	474 (29.6)	288 (33.9)
Walking speed (m/s), mean ± SD (missing n = 10)	0.7 ± 0.3	0.7 ± 0.2	0.9 ± 0.3
Walking speed groups, n (%)			
1.0 m/s or better	319 (12.2)	188 (11.7)	226 (26.6)
0.8 to <1 m/s	633 (24.2)	361 (22.5)	276 (32.7)
0.4 to <0.8 m/s	1,430 (54.7)	874 (54.6)	305 (35.9)
<0.4 m/s or unable	221 (8.5)	177 (11.1)	41 (4.8)

* Abbreviations: BMI = body mass index; CVD = cardiovascular disease; HTN = hypertension; MVPA = moderate/vigorous physical activity (yes/no); NSAID = nonsteroidal antiinflammatory drugs (yes/no).

information, respectively, by fully conditional specification methods. These methods are optimal when data are missing at random and the proportion missing is less than 50%. Ten imputed data sets were generated so that the number of imputations were similar to the percentage of data missing one or more covariables. Separate analyses were carried out in each of the 10 imputed data sets; then estimated parameters from all imputed data sets were pooled to generate a single estimate according to Rubin's rules (22).

For model 3, effect modification of the associations of foot symptoms with mortality was considered for walking speed, in addition to sex, race, obesity, and diabetes. An interaction term was used between each foot symptom definition and each potential effect modifier and considered significant if *P* was less than 0.10. If statistically significant, the HR between foot symptom and mortality was shown by level of effect modifier.

For model 3, we also generated adjusted survival curves for foot symptoms definitions that were statistically significantly associated with mortality showing the survival experience of an average participant in the population from which JoCoOA was sampled.

RESULTS

Figure 1 provides a summary of the final analytic sample for the current analyses. Initially, 2,754 participants were identified from baseline; after removal of duplicate IDs (n = 12), missing foot symptom/severity information for both feet (n = 121), and missing vital status (n = 8), 2,613 participants were available for analysis. Those with missing baseline covariables (n=162), were not excluded. Three time points of data were available for 824 participants, two time points for 806 participants, and one time point for 983 participants (Figure 1).

At baseline, of the 2,613 participants, the mean age was 63 (range 45–102) years, the mean BMI was approximately 31 kg/m^2, and nearly half of the participants (42%) had at least one comorbidity (Table 1). Of these participants, approximately one third were Black and two thirds were women. Over half of participants (55%) had walking speeds between 0.4 and less than 0.8 m/s.

At first follow-up (n = 1,604) and at the second follow-up (n = 850), BMI remained around 31 kg/m^2. Most participants at the first follow-up continued to have one comorbidity count (46%), whereas those at the second follow-up had one to two comorbidities (40% and 38%, respectively), with the presence of HTN and CVD increasing across time. At the second follow-up, remaining participants had the fastest walking speeds with 27% at 1.0 or better, 32% at 0.8 to less than 1 m/s, and 36% at 0.4 to less than 0.8 m/s.

At baseline, 37% of participants had any foot symptoms, whereas 25% and 21% had any foot symptoms at first and second follow-ups, respectively (Table 2). This trend continues with

Table 2. Baseline foot symptom/severity categories, the Johnston County Osteoarthritis Project

	Baseline (1999–2004; n = 2,613)	First follow-up (2006–2010; n = 1,604)	Second follow-up (2013–2015; n = 850)
Foot symptoms/severity variables			
Any foot symptoms, n (%)	969 (37.1)	401 (25.0)	175 (20.6)
Any foot symptoms laterality, n (%)			
none	1644 (62.9)	1203 (75.0)	675 (79.4)
unilateral	198 (7.6)	111 (6.9)	44 (5.2)
bilateral	771 (29.5)	290 (18.1)	131 (15.4)
At least moderate severity foot symptoms, n (%)	637 (24.4)	255 (15.9)	121 (14.2)
At least moderate severity foot symptoms laterality, n (%)			
none	1976 (75.6)	1349 (84.1)	729 (85.8)
unilateral	167 (6.4)	84 (5.2)	45 (5.3)
bilateral	470 (18.0)	171 (10.7)	76 (8.9)
Foot symptoms' worst severity from either foot, n (%)			
none (0)	1644 (62.9)	1207 (75.2)	675 (79.4)
mild (1)	332 (12.7)	142 (8.9)	54 (6.4)
moderate (2)	409 (15.7)	181 (11.3)	45 (5.3)
severe (3)	228 (8.7)	74 (4.6)	76 (8.9)
Foot symptoms' severity count for both feet, n (%)			
0	1644 (62.9)	1207 (75.2)	675 (79.4)
1	68 (2.6)	53 (3.3)	18 (2.1)
2	360 (13.8)	128 (8.0)	42 (4.9)
3	61 (2.3)	35 (2.2)	35 (4.1)
4	296 (11.3)	132 (8.2)	28 (3.3)
5	21 (0.8)	9 (0.6)	8 (0.9)
6	163 (6.2)	40 (2.5)	44 (5.2)

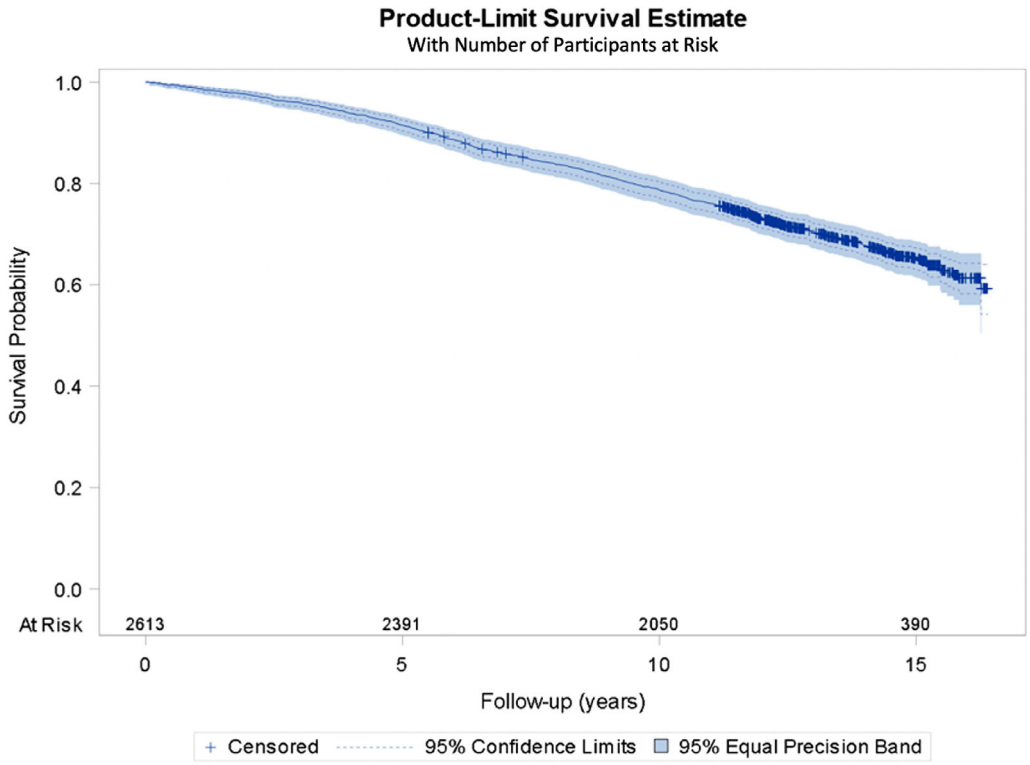
moderate foot symptoms. By first and second follow-ups, only 16% and 14% of participants remained with moderate foot symptoms compared with 24% at baseline. We also observed decreases in foot symptom severity over time, with 16% and 9% of participants experiencing moderate or severe foot symptoms, respectively at baseline. This is compared with 11% and 5% at first follow-up and 5% and 9% at second follow-up. Finally, we observed this same trend among those with bilateral moderate foot symptoms but not in those with unilateral moderate foot symptoms. At baseline, 18% of participants with moderate foot symptom severity experienced symptoms across both feet; at first and second follow-ups, this decreased to 11% and 9%, respectively.

An unadjusted Kaplan-Meier survival curve is presented in Figure 2. Although we would typically report median survival time, 69% of participants were censored, so we reported the quartile time to death instead (ie, the time when the first 25% of the sample had died). The curve shows those with foot symptoms had quartile time to death (0.75) of 11.4 years (95% CI 10.7–11.9) in which we observed 818 deaths overall (31% of JoCoOA).

In Figure 3, a Kaplan-Meier plot shows baseline moderate pain, aching, or stiffness (2) having a statistically significant difference from no or mild foot symptoms (1) (P = 0.0002). Moderate to severe foot symptoms show worse survival compared with mild or no symptoms.

Table 3 shows the aHRs from the time-dependent Cox proportional hazards models for the association of each of the six foot symptom definitions with time to death. For most of our foot symptom definitions, the effect of foot symptoms on hazard of death was independent of demographics (model 1), of risk factors and comorbidities (model 2), and of walking speed (model 3). The additional covariables did attenuate the HRs somewhat, but most definitions remained statistically significant between foot symptoms and death over follow-up—particularly those involving severity.

We examined effect modification with the main hypothesis that slower walking speed would modify the association seen between foot symptoms and time to death. Although slower walking speed significantly increased the hazard of mortality



Summary of the Number of Censored and Uncensored Values

Total	Failed	Censored	Percent Censored
2613	818	1795	68.69

Quarter time to death= 11.4 (95% CI 10.7, 11.9) years

Figure 2. Unadjusted Kaplan-Meier survival curve reporting quartile time to death. Abbreviation: CI = confidence interval.

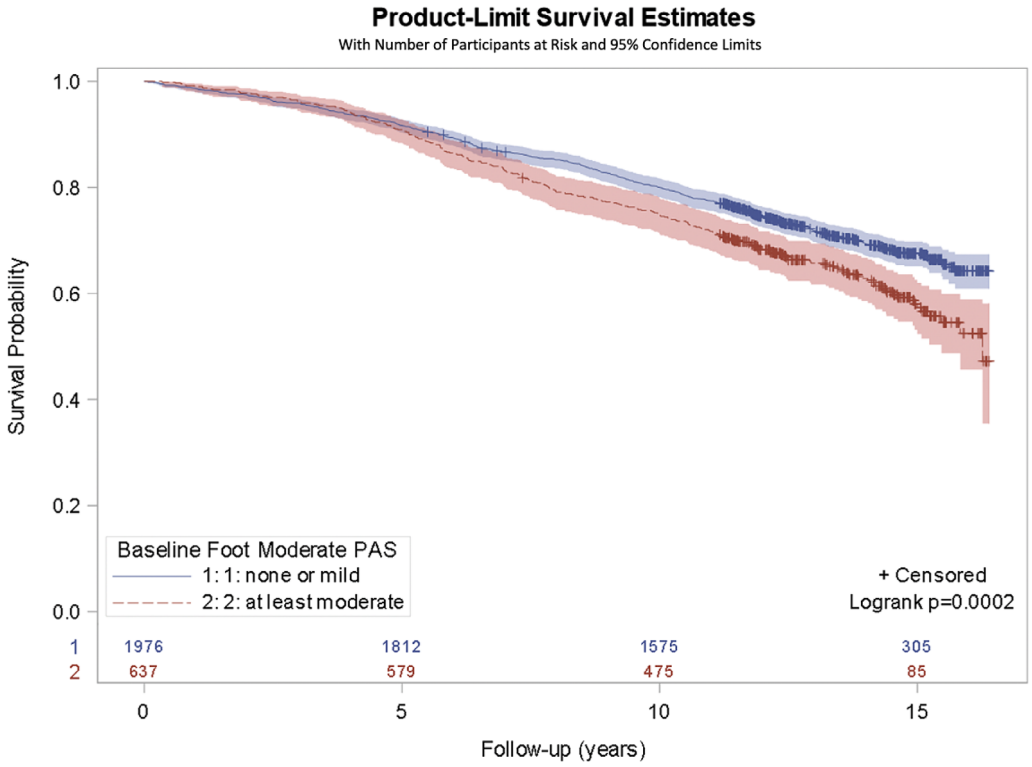


Figure 3. Kaplan-Meier plot showing baseline moderate PAS (2) and no or mild foot PAS (1). Abbreviation: PAS = pain, aching, stiffness.

Table 3. Adjusted HRs and 95% CIs for the association between foot symptoms and all-cause mortality over follow-up*

	Model by included covariables		
	Model 1	Model 2	Model 3
Model by foot symptom definition	HR (95% CI)	HR (95% CI)	HR (95% CI)
Any foot symptoms			
No foot symptoms	ref	ref	ref
Any foot symptoms	1.30 (1.12–1.50)	1.15 (0.99–1.35)	1.11 (0.95–1.29)
Laterality of foot symptoms			
No foot symptoms	ref	ref	ref
Any foot symptoms unilaterally	1.15 (0.89–1.51)	1.08 (0.83–1.41)	1.04 (0.79–1.36)
Any foot symptoms bilaterally	1.34 (1.15–1.57)	1.18 (1.00–1.40)	1.13 (0.95–1.34)
Severity of foot symptoms (grouped)			
None or mild severity foot symptoms	ref	ref	ref
At least moderate severity foot symptoms	1.52 (1.29–1.78)	1.34 (1.13–1.59)	1.30 (1.09–1.54)
Laterality of foot symptom severity			
None or mild severity foot symptoms	ref	ref	ref
At least moderate severity foot symptoms unilaterally	1.43 (1.09–1.89)	1.30 (0.98–1.72)	1.29 (0.97–1.71)
At least moderate severity foot symptoms bilaterally	1.55 (1.30–1.85)	1.36 (1.12–1.64)	1.30 (1.07–1.57)
Severity of foot symptoms			
No foot symptom severity	ref	ref	ref
Mild foot symptom severity	0.96 (0.75–1.22)	0.90 (0.71–1.15)	0.86 (0.68–1.10)
Moderate foot symptom severity	1.35 (1.11–1.64)	1.20 (0.98–1.47)	1.16 (0.95–1.43)
Severe foot symptom severity	1.86 (1.47–2.35)	1.58 (1.23–2.03)	1.48 (1.15–1.90)
Summed severity count of foot symptoms			
Symptom severity count for both feet (1 unit increase)	1.10 (1.06–1.15)	1.07 (1.03–1.12)	1.06 (1.02–1.10)

* Data used are multiply imputed (n = 10). Time-dependent Cox proportional hazard modeling time to death using the counting process for time-varying covariables. Model 1 (demographics): adjusted for birth cohort (strata), enrollment wave, age, sex, race, and education. Model 2 (comorbidities and relevant clinical risk factors): adjusted for model 1 + NSAIDs, smoking, alcohol use, MVPA, BMI, diabetes, five comorbidity count, knee PAS, and hip PAS. Model 3 (gait speed): adjusted for model 2 + gait speed categories.
Abbreviations: BMI = body mass index; CI = confidence interval; HR = hazard ratio; MVPA = moderate/vigorous physical activity; NSAID = nonsteroidal antiinflammatory drug; PAS = pain, aching, stiffness.

(compared with 1 m/s or better; HR, 95% CI for 0.8 m/s to <1 m/s: HR = 1.35, 0.88–2.07; 0.4 m/s to <0.8 m/s: HR = 2.60, 1.75–3.85; <0.4 m/s or unable: HR = 3.58, 2.33–5.48), there was no evidence of effect modification (interactions $P > 0.1$) between any of the six definitions of foot symptoms and walking speed. We also did not observe any effect modification between foot symptoms and the other variables considered (sex, race and ethnicity, obesity status, or diabetes status). In the fully adjusted model (model 3), no statistically significant associations were observed between mild or moderate foot symptom severity and mortality (HR = 0.86, 95% CI 0.68–1.10 and HR = 1.16, 95% CI 0.95–1.43, respectively). However, there was a significant association with severe foot symptom severity and mortality (HR = 1.48, 95% CI 1.15–1.90).

DISCUSSION

This community-based study found that the presence of at least moderate foot symptoms, independent of walking speed and many other potential confounding factors, was associated with a 30% to 48% increased hazard of reduced time to all-cause mortality in a large cohort of Black and White men and women. These effects were larger in those with greater symptom severity. Several definitions of foot symptoms were investigated, including any presence of pain, aching, or stiffness, foot symptom laterality, and measures of severity. A severity count across both feet was calculated because the presence of more severe symptoms or bilateral foot symptoms would likely have larger impacts on decreased walking speed compared with mild foot symptoms or unilateral foot symptoms. Although slower walking speeds continued to predict worse survival ($P < 0.0001$; data not shown), we did not find evidence that walking speed modified the effect of foot symptoms on mortality.

Previous studies have focused on hip or knee OA and pain in relation to mortality and may have been limited in the potential confounding factors considered in their analyses of OA to mortality (8–12). Our study is novel, in that to our knowledge, no previous studies have investigated the relationship of foot symptoms to mortality, and additionally, this study has adjusted for a wide variety of confounding factors, which may mediate effects on time to mortality. Even after adjustment for demographics including age, sex, race and ethnicity, and education, the effect of foot symptoms continued to predict mortality. Even further adjustment for other factors, including physical activity level, BMI, or comorbidities, as well as pain, aching, or stiffness at the knee or hip, did not explain away the association between foot symptoms on time to mortality in our study.

The effect of foot symptoms on mortality was independent of walking speed in this study. Master et al previously used data from JoCoOA with recorded 8-foot walk times (2.4 meters) to examine the association of walking speed with mortality risk over 9 years. They found a 23% higher hazard of mortality in those with symptomatic knee radiographic OA and proposed that walking difficulty may modify this relation (14). We did not find walking speed to be a moderator of the effect of foot symptoms on mortality, suggesting that poor mobility is not the explanation for the observed association.

Our results show a statistically significant and persistent relationship between foot symptoms and time to all-cause mortality; however, the underlying cause of this relationship remains unclear. Previous studies have shown that chronic pain, which is most often musculoskeletal in etiology (23), was significantly associated with mortality (24,25), but these studies have been inconsistent in analyzing for sociodemographic factors and differentiating arthritis from other causes of chronic pain. Torrance et al found that severe chronic pain was significantly associated with all-cause mortality (HR = 1.49, 99% CI 1.21–1.84) independent of sociodemographic factors including age, sex, marital status, education, and housing (25). However, almost half of the participants had chronic pain due to arthritis, and among those with arthritis, there was no significant association found between chronic pain and overall mortality. Self-reported chronic musculoskeletal pain in a large prospective population-based study of middle-aged women was associated with increased risk of mortality (HR = 2.1, 95% CI 1.1–4.2) (24). Notably, there was no difference in death from CVD or cancer between pain-free individuals compared with those with chronic pain. Torrance et al did not account for other confounding factors, including depression, comorbidity, lifestyle factors, social factors, and the duration of pain at baseline. Additionally, they stated that individuals with chronic pain have a less healthy lifestyle, are less physically active, smoke more, and belong to a lower social class, which they believe may be important confounders (24). Our study was able to include these potential confounders, and we did not observe that the effect of foot symptoms on mortality was altered by these factors. Additional studies in other populations should examine the presence of chronic foot pain and mortality to determine whether findings are consistent or differ. Moreover, the presence of anxiety and depression has been observed in around a third of patients with chronic foot and ankle diseases (26), and individuals with foot symptoms are more likely to report depressive symptoms (27). Although we accounted for depression as a confounder, future studies may examine this relationship more closely in relation to mortality.

It is likely that the presence of foot symptoms and/or OA may impair balance and muscle strength within the lower extremities, similar to knee OA. Previous research has investigated the presence of symptomatic radiographic hip and/or knee OA characterized by pain, aching, or stiffness on most days in relation to fall risk (28). This study found an increased incidence of falls with increasing number of knee and/or hip joints with symptomatic OA. Examination of foot OA symptoms within these analyses would be an important next step because falls are a leading cause of morbidity and mortality in older adults and are associated with foot pain (21).

Our study had several limitations. Regarding participant data, duration of foot symptoms prior to study entry was not assessed. In future studies, information about foot symptoms prior to study entry would expand the knowledge of the observed association between foot symptoms and mortality. Because of our cohort study design, we were unable to capture incident foot symptoms as they occur because the study examinations at which participants provided foot symptoms information occurred at ~5-year cycles. Additionally, we did not include radiographic OA within our study because foot radiographs were not obtained for our cohort until 2013, significantly decreasing any possible follow-up time for assessing mortality. Additional investigations of the association of foot OA to mortality should include radiographs to compare symptomatic radiographic OA to asymptomatic radiographic OA. Another limitation may be our use of the 8-foot walk because in our study, participants were unable to decelerate past the 8-foot mark because of space limitations within the room. For future studies, we suggest using a larger space and having participants complete a short walk (eg, 8 feet) and a longer walk (eg, greater than 60 feet) to assess mobility and its relationship to foot symptoms and OA and mortality more accurately.

Finally, although we produced estimates of the direct effects of foot symptom severity on mortality and considered effect modifiers of this association, future studies could assess whether modifiable mediators (for example, weight, depression, physical function, sleep) of this association exist and estimate both direct and indirect effects of this association.

The major strength of our study was use of a large group of community-dwelling Black and White men and women with a long follow-up time and a wealth of well-characterized covariables, including walking speed. We were able to assess models controlling for several comorbid conditions as well as lifestyle factors and risk factors for OA in our analyses. Finally, we were able to use the data from multiple time points to analyze foot symptoms over time. Although foot symptoms were not collected prior to study entry, we did have a long-recorded period of foot symptoms, which is not seen in many previous studies.

In conclusion, foot symptoms, after adjustment for walking speed, sex, race and ethnicity, obesity status, or diabetes status, may signify a higher hazard of all-cause mortality in older adults. This is especially an issue for those with at least moderate to severe foot pain, aching, or stiffness. Although we continued to see the effects of foot symptoms on increased hazard of mortality with slower walking speed, we did not find any evidence of effect modification of this association by sex, race, obesity, diabetes, or walking speed. Health professionals may consider therapeutic management of foot pain, perhaps with a view towards chronic pain management in adults with foot symptoms to manage risks in these individuals. Furthermore, this study highlights the need for future investigations of modifiable factors that alleviate foot symptoms.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Golightly had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Harmon, Alvarez, Hannan, Callahan, Gates, Bowen, Menz, Nelson, Golightly.

Acquisition of data. Callahan, Nelson, Golightly.

Analysis and interpretation of data. Harmon, Alvarez, Hannan, Callahan, Gates, Bowen, Menz, Nelson, Golightly.

ADDITIONAL DISCLOSURES

Author Hannan received funding to her institution from Amgen, Inc. and serves on the Board of Directors for the Rheumatology Research Foundation; neither of these activities are related to the work reported in this project.

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